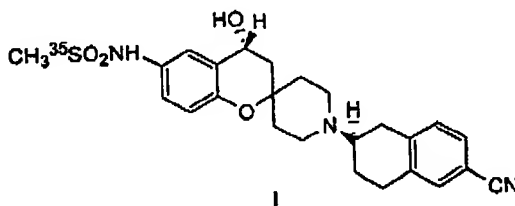


Amendments to the Claims:

Claims 1-4 (canceled)

Claim 5 (currently amended): A method for characterizing the activity of a compound as an I<sub>Kr</sub> channel blocker comprising contacting the test compound with a membrane containing the I<sub>Kr</sub> channel, derived from a cell line transfected with the human ERG gene, in the presence of the radioligand compound



or a pharmaceutically acceptable salt thereof,

monitoring whether the test compound influences the binding of the radioligand compound to the membrane containing the I<sub>Kr</sub> channel, and determining the I<sub>Kr</sub> channel blocker activity of the test compound.

Claim 6 (canceled)

Claim 7 (currently amended): The method as recited in Claim 6 5, wherein the cell line is HEK 293 cells or CHO cells.

Claim 8 (canceled)

Claim 9 (currently amended): The method as recited in Claim 8 7, wherein the radioligand compound of Formula I possesses a specific activity of in the range of about 900 Ci/mmol. to about 1498 Ci/mmol.

Claim 10 (currently amended): A method for assessing the binding of a test compound to a membrane containing the I<sub>Kr</sub> channel, derived from a cell line transfected with the human ERG gene, using a radioligand compound of Formula I, [<sup>35</sup>S]-radiolabeled (+)-N-[1'-(6-cyano-1,2,3,4-tetrahydro-2(R)-naphthalenyl)-3,4-dihydro-4(R)-hydroxyspiro[2H-1-benzopyran-2,4'-piperidin]-6-yl]-methanesulfonamide, comprising the steps of:

- 1) preparing solutions of the test compound at 5 or more different concentrations, a solution of control vehicle and a solution of (+)-N-[1'-(6-cyano-1,2,3,4-tetrahydro-2(R)-

- naphthalenyl)-3,4-dihydro-4(R)-hydroxySpiro[2H-1-benzopyran-2,4'-piperidin]-6-yl]-methanesulfonamide (compound of Formula II) in a solvent;
- 2) mixing the radioligand compound of Formula I with the membrane containing the IK<sub>r</sub> channel diluted with an assay buffer to form a membrane/radioligand mixture of known concentration;
  - 3) incubating a quantity of the membrane/radioligand mixture with the solution of test compound, control vehicle or compound of Formula II, as recited in Step 1, for a set time period at a temperature range of between about 40°C and about 37°C to give a mixture of membrane bound with the radioligand and the test compound, the control vehicle or the compound of Formula II;
  - 4) isolating from the incubated mixture the membrane bound with the radioligand and the test compound, the membrane bound with the radioligand and with the control vehicle or the membrane bound with the radioligand and the compound of Formula II;
  - 5) measuring the radioactivity of the isolated membrane bound with the radioligand and the test compound, the membrane bound with the radioligand and with the control vehicle or the membrane bound with the radioligand and the compound of Formula II;
  - 6) repeating steps 3 through 5 with the test compound at each concentration, the solution of control vehicle and the solution of the compound of Formula II, as recited in Step 1;
  - 7) calculating the IC<sub>50</sub> corresponding to the measured radioactivity of: 1) the membrane bound with the radioligand and each concentration of the test compound, 2) the membrane bound with the radioligand and with the control vehicle, and 3) the membrane bound with the radioligand and the compound of Formula II, to assess the binding of the test compound to the membrane.

Claim 11 (canceled)

Claim 12 (currently amended): The method as recited in Claim ~~11~~ 10, wherein the cell line is HEK 293 cells or CHO cells.

Claim 13 (canceled)

Claim 14 (currently amended): The method as recited in Claim ~~13~~ 12, wherein the solutions of the test compound are prepared in Step 1 at 7 different concentrations.

Claim 15 (original): The method as recited in Claim 14, wherein the time period for incubation in Step 3, is about 30 minutes to 1 hour.

Claim 16 (original): The method as recited in Claim 15, wherein the temperature for the incubation in Step 3, is room temperature (25°C).

Claim 17 (original): The method as recited in Claim 16, wherein the membrane-bound with radioligand or test compound is isolated in Step 4 with Unifilters, Scintillation Proximity Assay (SPA) beads or the Flashplates.

Claim 18 (original): The method as recited in Claim 17, wherein the membrane containing the  $I_{K_r}$  channel is derived from a HEK 293 cell line transfected with the human ERG gene.

Claim 19 (currently amended): The method as recited in Claim 8 18, wherein the radioligand compound of Formula I possesses a specific activity of in the range of about 900 Ci/mmol. to about 1498 Ci/mmol.

Claim 20 (currently amended): A method for assessing the binding of a test compound to a membrane containing the  $I_{K_r}$  channel derived from a cell line transfected with the human ERG gene, using a radioligand of Formula I, [ $^{35}\text{S}$ ]-radiolabeled (+)-N-[1'-(6-cyano-1,2,3,4-tetrahydro-2(R)-naphthalenyl)-3,4-dihydro-4(R)-hydroxy]spiro[2H-1-benzopyran-2,4'-piperidin]-6-yl]-methanesulfonamide, comprising the steps of:

- 1) preparing assay wells with 4  $\mu\text{l}$  of the test compound in dimethylsulfoxide (DMSO) diluted 100x with assay buffer at 5 or more different concentrations, a control vehicle of DMSO and a DMSO solution of (+)-N-[1'-(6-cyano-1,2,3,4-tetrahydro-2(R)-naphthalenyl)-3,4-dihydro-4(R)-hydroxy]spiro[2H-1-benzopyran-2,4'-piperidin]-6-yl]-methanesulfonamide (compound of Formula II);
- 2) adding the radioligand compound of Formula I at 50pM to the membrane containing the  $I_{K_r}$  channel diluted with assay buffer to form a membrane/radioligand mixture;
- 3) incubating each assay well with 400  $\mu\text{l}$  of the 50 pM membrane/radioligand mixture for about 75 minutes to about 90 minutes at room temperature (25°C) to give assay wells containing the membrane bound with the radioligand and the test compound at each concentration, the DMSO control vehicle or the compound of Formula II where the final concentration of the membrane containing the  $I_{K_r}$  channel is 11  $\mu\text{g}/\text{ml}$ ;
- 4) filtering the incubated assay wells through 0.1% BSA presoaked filters to isolate on the filters the membrane bound with the radioligand and the test compound at each concentration, the DMSO control vehicle or the compound of Formula II;
- 5) washing each of the filters containing the membrane bound with the radioligand and the test compound at each concentration, the DMSO control vehicle or the compound of Formula II about 5 times with 500  $\mu\text{l}$  of ice cold wash buffer;

- 6) drying the washed-filters containing the membrane bound with the radioligand and the test compound at each concentration, the DMSO control vehicle or the compound of Formula II at room temperature in a fume hood;
- 7) adding 50 TI Microscint-20 microscintillate to the dried-filters containing the membrane bound with the radioligand and the test compound at each concentration, the DMSO control vehicle or the compound of Formula II;
- 8) measuring the microscintillation count of the microscintillation-treated filters containing the membrane bound with the radioligand and the test compound at each concentration, the DMSO control vehicle or the compound of Formula II for one minute; and
- 9) calculating the IC<sub>50</sub> corresponding to the measured microscintillation count of: 1) the microscintillation-treated filters containing the membrane bound with the radioligand and each concentration of the test compound, 2) the microscintillation-treated filters containing the membrane bound with the radioligand and with the control vehicle, and 3) the microscintillation-treated filters containing the membrane bound with the radioligand and the compound of Formula II.

Claim 21 (canceled)

Claim 22 (currently amended): The method as recited in Claim ~~24~~ 20, wherein the cell line is HEK 293 cells.

Claim 23 (canceled)

Claim 24 (currently amended): The method as recited in Claim ~~23~~ 22, wherein the solutions of the test compound are prepared in Step 1 at 7 different concentrations.

Claim 25 (canceled)

Claim 26 (currently amended): The method as recited in Claim ~~25~~ 24, wherein the radioligand compound of Formula I possesses a specific activity of in the range of about 900 Ci/mmol. to about 1498 Ci/mmol.

Claim 27 (original): The method as recited in Claim 26, wherein the membrane-bound with radioligand or test compound is filtered in Step 4 with Unifilters.

Claims 28-40 (canceled)